AWARD NUMBER: W81XWH-12-1-0497

TITLE: Phospholipids as Biomarkers for Excessive Alcohol Use

PRINCIPAL INVESTIGATOR:

Suthat Liangpunsakul, MD
Associate Professor of Medicine

CONTRACTING ORGANIZATION:

Division of Gastroenterology and Hepatology
Department of Medicine
Indiana University School of Medicine

REPORT DATE: October 2015

TYPE OF REPORT: Annual report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2015	Annual	15Sept2014 - 14Sep2015

4. TITLE AND SUBTITLE
Phospholipids as Biomarkers for Excessive Alcohol Use

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-12-1-0497

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Suthat Liangpunsakul

Email: sliangpu@iu.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Trustees of Indiana University
Indianapolis, IN 46202

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT **Our proposal is to determine the diagnostic utility of sphingomyelin (SM) and lysophosphatidylcholine (LPC) as the potential biomarkers to screen for excessive alcohol use (EAU); a rising epidemic reported to be as high as 40% among returning veterans. Drinking becomes excessive when it causes or elevates the risk for alcohol-related problems or complicates the management of other health problems. According to the NIH/NIAAA, excessive drinking is defined as men who drink more than 4 standard drinks in a day (or more than 14 per week) and women who drink more than 3 drinks in a day (or more than 7 per week). Non-civilian military personnel have been deployed in support of the war efforts in Afghanistan (Operation Enduring Freedom, OEF) and Iraq (Operation Iraqi Freedom, OIF) since September 11, 2001. These sustained combat operations have resulted in military personnel experiencing physical threat or actual injury during the deployment and difficult adjustments during post-deployment period. Negative life stress is a major contributor to the onset and exacerbation of EAU. The prevalence of EAU is alarming, and the vigilance and action to identify veterans with EAU is of importance. The consequences of under-detection of EAU, thus delayed intervention are serious because relative risk of alcohol-related health conditions such as cirrhosis, pancreatitis, and hepatocellular carcinoma, is increased with the amounts and duration of alcohol consumed per day. We hypothesize that alcohol consumption elevates a panel of serum phospholipids (sphingomyelin, and lysophosphatidylcholines) in proportion to the level of consumption in the past month.**

15. SUBJECT TERMS
Nothing listed

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
U	U	U	UU	6	USAMRMC

Table of Contents

Page

INTRODUCTION:

Our proposal is to determine the diagnostic utility of sphingomyelin (SM) and lysophosphatidylcholine (LPC) as the potential biomarkers to screen for excessive alcohol use (EAU); a rising epidemic reported to be as high as 40% among returning veterans. Drinking becomes excessive when it causes or elevates the risk for alcohol-related problems or complicates the management of other health problems. According to the NIH/NIAAA, excessive drinking is defined as men who drink more than 4 standard drinks in a day (or more than 14 per week) and women who drink more than 3 drinks in a day (or more than 7 per week). Non-civilian military personnel have been deployed in support of the war efforts in Afghanistan (Operation Enduring Freedom, OEF) and Iraq (Operation Iraqi Freedom, OIF) since September 11, 2001. These sustained combat operations have resulted in military personnel experiencing physical threat or actual injury during the deployment and difficult adjustments during post-deployment period. Negative life stress is a major contributor to the onset and exacerbation of EAU. The prevalence of EAU is alarming, and the vigilance and action to identify veterans with EAU is of importance. The consequences of under-detection of EAU, thus delayed intervention are serious because relative risk of alcohol-related health conditions such as cirrhosis, pancreatitis, and hepatocellular carcinoma, is increased with the amounts and duration of alcohol consumed per day. We hypothesize that alcohol consumption elevates a panel of serum phospholipids (sphingomyelin, and lysophosphatidylcholines) in proportion to the level of consumption in the past month. Further, we hypothesize that such relationship can also be identified from a dried blood spot via a finger-stick procedure. The *central objective* of this proposal is to determine the diagnostic values of these two phospholipids as the potential biomarkers for EAU. We plan to recruit subjects to determine the relationship between the panel of serum phospholipids of interest and the amount of alcohol consumption during the past month in returning Indiana OEF/OIF veterans.

KEYWORDS: Excessive alcohol use, phospholipids, biomarkers

OVERALL PROJECT SUMMARY:

Recruitment: Since the inception of the study, we do not experience any problems with subjects' recruitment. To date, we have completed the recruitment for Part I and II. We are now working on the data entry as well as creating the data sheet for analysis. We are now in preparation for analysis of all the samples we collected which will take another 6-9 months.

KEY RESEARCH ACCOMPLISHMENTS: Nothing to report at this stage

CONCLUSION: Our project is significant to military personnel including the veterans. If successful, we expect to identify the non-invasive markers that can be used in clinical practice to screen for excessive alcohol use.

PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:

I would like to thank the DoD for support of my research. Because of the protected time that I received, I would be able to use this time to publish several papers (cited the DoD support) below.

1. Gough G, Heathers L, Puckett D, Westerhold C, Ren X, Yu Z, Crabb DW, Liangpunsakul S. The Utility of Commonly Used Laboratory Tests to Screen for Excessive Alcohol Use in Clinical Practice. Alcohol Clin Exp Res. 2015 Jun 25. doi: 10.1111/acer.12780. [Epub ahead of print] PubMed PMID: 26110815.
2. Liangpunsakul S, Lai X, Ross RA, Yu Z, Modlik E, Westerhold C, Heathers L, Paul R, O'Connor S, Crabb DW, Witzmann F. Novel serum biomarkers for detection of excessive alcohol use. Alcohol Clin Exp Res. 2015 Mar;39(3):556-65. doi: 10.1111/acer.12654. Epub 2015 Feb 19. PubMed PMID: 25704570; PubMed Central PMCID: PMC4348329.
3. Lai X, Liangpunsakul S, Li K, Witzmann FA. Proteomic profiling of human sera for discovery of potential biomarkers to monitor abstinence from alcohol abuse. Electrophoresis. 2015 Feb;36(4):556-63. doi: 10.1002/elps.201400319. Epub 2015 Jan 22. PubMed PMID: 25475211; PubMed Central PMCID: PMC4492280.
4. Liangpunsakul S, Bennett R, Westerhold C, Ross RA, Crabb DW, Lai X, Witzmann FA. Increasing serum pre-adipocyte factor-1 (Pref-1) correlates with decreased body fat, increased free fatty acids, and level of recent alcohol consumption in excessive alcohol drinkers. Alcohol. 2014 Dec;48(8):795-800. doi:10.1016/j.alcohol.2014.07.013. Epub 2014 Sep 28. PubMed PMID: 25449367; PubMed Central PMCID: PMC4254533.
5. Zhou P, Werner JH, Lee D, Sheppard AD, Liangpunsakul S, Duffield GE. Dissociation between diurnal cycles in locomotor activity, feeding behavior and hepatic PERIOD2 expression in chronic alcohol-fed mice. Alcohol. 2015 Jun;49(4):399-408. doi: 10.1016/j.alcohol.2015.03.005. Epub 2015 Apr 23. PubMed PMID: 25960184; PubMed Central PMCID: PMC4495663.
6. Liangpunsakul S. ChREBP, SIRT1 and ethanol metabolism- a complicated network in alcohol-induced hepatic steatosis. Hepatology. 2015 Jun 4. doi: 10.1002/hep.27926. [Epub ahead of print] PubMed PMID: 26044569.
7. Zhou P, Ross RA, Pywell CM, Liangpunsakul S, Duffield GE. Disturbances in the murine hepatic circadian clock in alcohol-induced hepatic steatosis. Sci Rep. 2014 Jan 16;4:3725. doi: 10.1038/srep03725. PubMed PMID: 24430730; PubMed Central PMCID: PMC3893658.
8. Tao R, Xiong X, Liangpunsakul S, Dong XC. Sestrin 3 protein enhances hepatic insulin sensitivity by direct activation of the mTORC2-Akt signaling. Diabetes. 2015 Apr;64(4):1211-23. doi: 10.2337/db14-0539. Epub 2014 Nov 5. PubMed PMID: 25377878; PubMed Central PMCID: PMC4375082.
9. Chayanupatkul M, Liangpunsakul S. Alcoholic hepatitis: a comprehensive review of pathogenesis and treatment. World J Gastroenterol. 2014 May 28;20(20):6279-86. doi: 10.3748/wjg.v20.i20.6279. Review. PubMed PMID: 24876748; PubMed Central PMCID: PMC4033465.
10. Jinjuvadia R, Liangpunsakul S; Translational Research and Evolving Alcoholic Hepatitis Treatment Consortium. Trends in Alcoholic Hepatitis-related Hospitalizations, Financial Burden, and Mortality in the United States. J Clin Gastroenterol. 2015 Jul;49(6):506-11. doi: 10.1097/MCG.0000000000000161. PubMed PMID: 25198164; PubMed Central PMCID: PMC4276725.
11. Chayanupatkul M, Liangpunsakul S. Cirrhotic cardiomyopathy: review of pathophysiology and treatment. Hepatol Int. 2014 Jul;8(3):308-15. doi: 10.1007/s12072-014-9531-y. PubMed PMID: 25221635; PubMed Central PMCID: PMC4160726.

INVENTIONS, PATENTS AND LICENSES: N/A

REPORTABLE OUTCOMES: Nothing to report at this time

OTHER ACHIEVEMENTS: Nothing to report

If you have any questions or concerns, please do not hesitate to contact me.

Sincerely,

Suthat Liangpunsakul, MD, MPH
Associate Professor of Medicine
Division of Gastroenterology and Hepatology
Department of medicine
Indiana University School of Medicine

Adjunct, Associate Professor of Public Health
Department of Public Health
Indiana University Purdue University Indianapolis